Development of a Noninvasive Prenatal Test for Beta-Hemoglobinopathies for Earlier Stem Cell Therapeutic Interventions

Grant Award Details

Development of a Noninvasive Prenatal Test for Beta-Hemoglobinopathies for Earlier Stem Cell Therapeutic Interventions

Grant Type: Diagnostic Translational Research Projects

Grant Number: TRAN2-10990-B

Project Objective: Development of a CLIA-certified Non Invasive Prenatal Test for β-hemoglobinopathies using next-generation sequencing

Investigator:

Name:	Steven Mack
Institution:	University of California, San Francisco
Type:	PI

Disease Focus: Beta Thalassemia, Blood Disorders, Sickle Cell Disease

Human Stem Cell Use: Adult Stem Cell

Award Value: $653,234

Status: Active

Grant Application Details

Application Title: Development of a Noninvasive Prenatal Test for Beta-Hemoglobinopathies for Earlier Stem Cell Therapeutic Interventions

Public Abstract:

Translational Candidate

An earlier, safer noninvasive prenatal screening test for β-thalassemia and sickle cell disease to identify candidates for prenatal stem cell therapy

Area of Impact

Our test is safer and can be conducted earlier than the current methods of prenatal testing (e.g. chorionic villous sampling and amniocentesis)

Mechanism of Action

Our test uses next generation sequencing to analyze fetal DNA in a mother's blood in order to screen for β-thalassemia and sickle cell anemia. Counting sequence reads and comparing observed and expected values for the β-globin mutations allows the inference of fetal genotype. If the test is negative (fetus unaffected), the mother will be spared the invasive testing. If the test is positive (fetus affected), confirmatory testing can be pursued and stem cell therapeutic interventions considered.

Unmet Medical Need

The availability of a safer and earlier fetal diagnosis, such as that afforded by our NIPT assay, will remove a critical bottleneck and greatly facilitate hematopoietic stem cell (HSC) transplants, currently the only curative therapy for the hemoglobinopathies.

Project Objective

Assay ready for validation in CLIA-certified lab

Major Proposed Activities

- Optimization of NIPT assay for autosomal recessive disorders and establishing cut-offs to develop an algorithm and software
- Testing of performance characteristics to demonstrate analytical sensitivity, specificity, precision, and repeatability adequate for intended use
- Demonstration of analytical accuracy on well characterized clinical samples and development of a clinical validation plan that meets CLIA requirements

Statement of Benefit to California:

California boasts one of the most ethnically diverse populations of the United States. The incidence of mutations causing diseases such as sickle cell disease, alpha-thalassemia, and beta-thalassemia, per 100,000 infants screened in California are 15.2, 11.1, and 1.8, respectively. As curative therapies involving stem cell transplants and gene editing become more readily available (after birth and intrauterine), earlier and safer fetal diagnosis will be critical for their implementations.
